

Inpatients versus outpatients with advanced non-small cell lung cancer: Characteristics and outcomes



Joanna Gotfrit^{a,b}, Caleb Jonker^c, Tinghua Zhang^c, Glenwood Goss^{a,b,c}, Garth Nicholas^{a,b,c}, Scott Laurie^{a,b,c}, Paul Wheatley-Price^{a,b,c,*}

^a Department of Medicine, University of Ottawa, 501 Smyth Road, Ottawa, Ontario K1H 8L6, Canada

^b Ottawa Hospital Cancer Centre, Ottawa, 501 Smyth Road, Ottawa, Ontario K1H 8L6, Canada

^c Ottawa Hospital Research Institute, 725 Parkdale Avenue, Ottawa, Ontario K1Y4E9, Canada

ARTICLE INFO

Keywords:

Lung cancer
Referral
Systemic therapy
Hospitalized
Survival

ABSTRACT

Background: Most newly diagnosed advanced NSCLC patients have an initial medical oncology consult as an outpatient. Sometimes, the initial consult occurs as an inpatient. We explored differences among NSCLC patients presenting to medical oncology while hospitalized versus as outpatients.

Methods: With ethics approval, we performed a retrospective analysis of all stage IIIB and IV NSCLC patients at our institution consulted by medical oncology between 2009 and 2012. The primary analysis is descriptive, exploring differences in baseline characteristics, treatment choices, and overall survival (OS).

Results: In total, 637 patients were included: 123 inpatients and 514 outpatients. Among outpatients, 55% received systemic therapy compared to 21% of inpatients. Among treated patients, inpatients were likely to be younger (81% vs 70% <70 years, $p = 0.04$), have PS 3–4 (38% vs 5%, $p < 0.001$), have $\geq 5\%$ weight loss (54% vs 42%, $p = 0.01$), anemia (19% vs 4%, $p = 0.001$), leukocytosis (38% vs 32%, $p = 0.001$), thrombocytosis (27 vs 23%, $p = 0.001$), renal dysfunction (12% vs 5%, $p = 0.01$) and more rapid onset of symptoms (27% vs 6% for <2 weeks, 35% vs 11% for 2–6 weeks; $p < 0.001$). Inpatients who received systemic therapy were more likely to have a complete or partial response (42% vs 26%, $p = 0.007$), however had a shorter median OS than treated outpatients (8.4 vs 10.5 months, $p = 0.003$).

Conclusions: Patients initially consulted by medical oncologists while hospitalized were more unwell and fewer received systemic therapy. However, if treated, they had higher response rates than outpatients and reasonable OS. Systemic therapy can be considered in hospitalized advanced NSCLC patients.

Microabstract: A minority of patients with lung cancer have an initial oncology consultation as an inpatient. We compared the characteristics and outcomes of inpatients with their outpatient counterparts. Inpatients were more unwell at diagnosis and fewer received systemic therapy, but among those who did, they were more likely to respond and their overall survival approached that of the outpatient cohort.

Introduction

Lung cancer poses a significant health burden in Canada. One in 12 men and 1 in 15 women develop lung cancer in their lifetime. Further, lung cancer is the leading cause of cancer death. An estimated 20,800 people died of lung cancer in Canada in 2016 accounting for approximately 26% of all cancer deaths [1].

A majority of patients with non-small cell lung cancer (NSCLC) present with advanced (stage IIIB or IV) disease, and many who receive curative therapy for early stage disease will subsequently relapse. Patients with advanced disease are frequently referred to medical

oncologists to discuss systemic therapy options, although it should be noted that a significant minority may never actually see a medical oncologist [2].

The referral to medical oncology for a new diagnosis of a lung malignancy usually occurs through the outpatient department [3]. For this reason, the majority of published data on the diagnosis and treatment of patients with new advanced lung cancer reflects the outpatient population. However, a significant proportion of patients may be admitted to the hospital at the time of their first medical oncology consultation. We have previously published a descriptive analysis of patients with advanced NSCLC seen for the first time by medical

* Corresponding author at: The Ottawa Hospital Cancer Centre, 501 Smyth Road, Ottawa, Ontario K1H 8L6, Canada.

E-mail address: pwheatleyprice@toh.ca (P. Wheatley-Price).

oncologists while hospitalized [4]. This group of patients is inherently sick, is unlikely to receive systemic therapy and may be nearing the end of life at the time of their first consultation. To our knowledge, no literature directly comparing the inpatient and outpatient advanced NSCLC populations exists.

With the goal of better understanding the differences among patients presenting to medical oncologists through the inpatient vs outpatient departments, we undertook a single-institution retrospective chart review at our tertiary care hospital to compare the characteristics and outcomes of patients with advanced NSCLC presenting to medical oncologists through the inpatient department compared to the outpatient department.

Materials and methods

With local research ethics board approval, we performed a retrospective single-centre chart review of all patients with advanced NSCLC at our institution who were seen by medical oncologists as inpatients and outpatients for the first time from 2009–2012. Only patients with histologically-confirmed NSCLC were included in the analysis. Patients were included if they had stage IIIB (palliative intent) or stage IV NSCLC at the initial consult (or that stage established as the result of investigations initiated at the same time). Patients receiving curative therapy and those who had been treated with curative intent for NSCLC and then referred on relapse were excluded. The full methods and outcomes from treatment for both the inpatient and outpatient populations have been previously described [4,5].

Briefly, baseline data on patient demographics, laboratory assessments, clinical assessments, disease characteristics and treatment with systemic therapy and radiotherapy were recorded. The Eastern Cooperative Oncology Group (ECOG) performance status (PS) [6], when not recorded directly in the clinical notes, was estimated from the clinical assessment at the time of the first medical oncology consultation. For treated patients, response was assessed using RECIST criteria, version 1.1 [7].

This was a descriptive and exploratory analysis. The objectives were to describe the clinical characteristics of the advanced NSCLC population stratified by inpatient or outpatient status at the time of presentation to medical oncology and to determine whether mode of presentation was associated with uptake of systemic therapy and overall survival (OS). The primary objective was to compare OS between the inpatient and outpatient groups, with OS defined as the time from histologic diagnosis to death or last known follow-up. The secondary objectives were to analyze uptake of systemic therapy, response rate and survival in patients who received systemic therapy. The Kaplan-Meier method and Cox proportional hazards modelling were used for the survival analysis. Univariate and multivariate logistic regression was performed to identify factors associated with receiving systemic therapy. All data points collected went into the model. Only factors significantly associated with the outcomes of interest in the univariate analyses were included in the multivariate analyses. Lactate dehydrogenase (LDH) was excluded from the multivariate survival analyses due to substantial missing data. All statistical analyses were performed using SAS software version 9.3 (SAS Institute Inc., Cary, NC).

Results

Demographics

Overall 637 patients were included, 123 inpatients and 514 outpatients. Comparing baseline demographics of patients seen for the first time by medical oncology as inpatients vs outpatients respectively, age was similar (65 vs 68 years old, $p = 0.75$), fewer were male (44% vs 56%, $p = 0.017$) and more were PS 3–4 (74% vs 22%, $p < 0.001$). Presentation leading to histologic diagnosis was significantly different among inpatients vs outpatients ($p = 0.03$). Inpatients were more likely

Table 1
Baseline demographics of inpatients and outpatients.

Demographic	Inpatients ^a		Outpatients ^b		P-value
	N	%	N	%	
Age at diagnosis					0.75
< 70	73	59	297	58	
≥ 70	50	41	217	42	
Median (range)	65 (23–85)		68 (35–90)		0.34
Gender					0.017
Male	54	44	287	56	
Female	69	56	227	44	
PS					< 0.001
0–2	21	17	363	71	
3–4	91	74	111	22	
Unknown	11	9	40	8	
Smoking status					0.0071
Current	55	45	219	43	
Ex-smoker	50	41	253	49	
Never smoked	11	9	36	7	
Unknown	7	6	6	1	
Smoking pack-years					0.50
Median (range)	40 (0–120)		40 (0–200)		
Bloodwork at consult					
Hb < 100 g/L	28	23	27	5	< 0.001
Cr > 120 μmol/L	17	14	38	7	0.019
WBC count > 11 × 10 ⁹ /L	75	61	180	35	< 0.001
Platelets > 400 × 10 ⁹ /L	36	39	128	25	0.20
LDH > 250	7	6	51	10	< 0.001
Presentation leading to histologic diagnosis					
Local symptoms	91	74	357	69	0.03
Constitutional symptoms	12	10	27	5	
Incidental/Other	20	16	130	25	
Onset of symptoms					< 0.001
< 2 weeks	29	24	27	5	
2–6 weeks	27	22	67	13	
6 weeks–6 months	43	35	260	51	
> 6 months	15	12	105	20	
Unknown	9	7	55	11	
Constitutional symptoms					< 0.001
Yes	77	63	319	62	
No	21	17	176	34	
Unknown	25	20	19	4	
Weight loss					< 0.001
< 5%	21	17	224	44	
≥ 5%	69	56	252	49	
Unknown	33	26	38	7	
Histologic subtype					0.63
Squamous	30	24	115	22	
Non-Squamous	93	76	399	78	
Stage					0.13
IIIB	13	11	34	6	
IV	110	89	480	93	
Presence of brain mets at diagnosis					0.85
Yes	35	28	142	28	
No	88	72	372	72	
Days from histologic diagnosis to medical oncology consult					< 0.001
Median (range)	9 (–2–98)		25 (–23–161)		

Data are presented as n (%) except where otherwise noted. Percentages as reported are rounded to the nearest whole number.

Abbreviations: PS performance status, Hb Hemoglobin, Cr Creatinine, WBC while blood cell, mets metastases.

^a Inpatients designates patients whose first consultation by medical oncology occurred as an inpatient.

^b Outpatients designates patients whose first consultation by medical oncology occurred as an outpatient.

present with local symptoms (74% vs 69%) and constitutional symptoms (10% vs 5%) and less likely to present incidentally (16% vs 25%). The time interval from symptom onset to diagnosis was significantly shorter among inpatients vs outpatients ($p < 0.001$). Inpatients were more likely to be diagnosed within 2 weeks of symptom onset (24% vs 5%) and within 2–6 weeks of symptom onset (22% vs 13%) compared

to outpatients. Inpatients were more likely to have $\geq 5\%$ weight loss (56% vs 49%, $p < 0.001$). There was no difference between inpatients and outpatients for stage at diagnosis or histologic subtype. Inpatients had a shorter time interval from histologic diagnosis to first medical oncology consultation (9 vs 25 days, $p < 0.001$). See Table 1 for patient demographics stratified by inpatients vs outpatients.

Treatment characteristics

Overall 308 patients (48% of the overall cohort) received systemic therapy. Systemic therapy included platinum doublets, cytotoxic monotherapy and tyrosine kinase inhibitors. Among outpatients, 55% received systemic therapy compared to only 21% of inpatients ($p < 0.001$). Among patients who received systemic therapy, there was no significant difference in type of treatment received (platinum doublet, cytotoxic monotherapy, or tyrosine kinase inhibitor) for inpatients vs outpatients in any line of therapy. Comparing inpatients who received systemic therapy and outpatients who received systemic therapy respectively, inpatients were more likely to be younger (81% vs 70% were < 70 years old, $p = 0.04$), have PS 3–4 (38% vs 5%, $p < 0.001$) and have lab work abnormalities including hemoglobin < 100 g/L (19% vs 4%, $p < 0.001$), creatinine > 120 $\mu\text{mol/L}$ (12% vs 5%, $p = 0.011$), leukocytosis $> 11 \times 10^9/\text{L}$ (38% vs 32%, $p < 0.001$) and thrombocytosis $> 400 \times 10^9/\text{L}$ (27% vs 23%, $p < 0.001$). More rapid onset of symptoms leading to diagnosis occurred among treated inpatients ($p < 0.001$). Treated inpatients were more likely to be diagnosed within 2 weeks of symptoms onset (27% vs 6%) and within 2–6 weeks of symptom onset (35% vs 11%). Treated inpatients had more weight loss $\geq 5\%$ (54% vs 42%, $p = 0.012$). Stage at diagnosis and histologic subtype was similar among treated inpatients and outpatients. Treated inpatients had a shorter time interval from histologic diagnosis to first medical oncology consultation (7 vs 23 days, $p < 0.001$).

Comparing patients presenting to medical oncology as inpatients vs outpatients respectively, the stated reason that inpatients did not receive systemic therapy was more often poor PS (77% vs 66%, $p < 0.001$). Among treated patients, a similar number of lines of therapy ($p = 0.23$) was given to inpatients vs outpatients (15% vs 31% received 1 line, 3% vs 14% received 2 lines, 1% vs 8% received 3 lines). Notably, inpatients who received 1st line systemic therapy were more likely to have a complete or partial response compared to outpatients who received systemic therapy (42% vs 26%, $p = 0.007$). Inpatients had a shorter interval from histologic diagnosis to first systemic treatment (44 vs 53 days, $p = 0.05$) but a similar interval from medical oncology consultation to first systemic treatment (30 vs 24 days, $p = 0.57$). Inpatients were less likely to receive palliative radiotherapy (72% vs 81%, $p = 0.03$).

See Table 2 for factors associated with receiving palliative systemic therapy in univariate and multivariate analysis. Factors that significantly decreased the likelihood of receiving systemic therapy in univariate analysis include age at diagnosis ≥ 70 , anemia, renal dysfunction, leukocytosis, constitutional symptoms, PS 3–4, weight loss and being an inpatient at time of first consultation. Factors that remained significant in multivariate analysis include age at diagnosis ≥ 70 , leukocytosis and constitutional symptoms. Inpatient status was not a predictor of decreased likelihood for receiving systemic therapy in multivariate analysis.

Survival analysis

Median OS for the whole cohort was 6.1 months (95% CI 5.4–6.9). For patients receiving or not receiving systemic therapy respectively, OS was 10.3 months (95% CI 9.4–11.1) vs 3.1 months (95% CI 2.7–3.5), p -value < 0.001 . For inpatients vs outpatients respectively, OS was 2.1 months (95% CI 1.5–2.3) vs 7.2 months (95% CI 6.4–8.1), $p < 0.001$. Among patients treated with systemic therapy, OS for inpatients vs

Table 2
Factors associated with decreased likelihood of receiving palliative systemic therapy in the overall cohort.

Factor	Univariate analysis			Multivariate analysis		
	OR	95% CI	P-value	OR	95% CI	P-value
Age at diagnosis ≥ 70	0.36	0.26–0.49	< 0.001	0.30	0.19–0.47	< 0.001
Baseline Hb < 100	0.43	0.24–0.78	0.006	0.98	0.39–2.45	0.96
Baseline Cr ≥ 120	0.47	0.26–0.85	0.012	0.81	0.36–1.8	0.60
Baseline WBC ≥ 11	0.51	0.37–0.71	< 0.001	0.498	0.31–0.79	0.003
Constitutional symptoms	0.33	0.23–0.47	< 0.001	0.67	0.39–1.14	0.14
PS 3–4	0.064	0.04–0.10	< 0.001	0.076	0.042–0.14	< 0.001
Weight loss $> 5\%$	0.43	0.31–0.61	< 0.001	0.86	0.51–1.46	0.58
Inpatient at first consult	0.22	0.14–0.35	< 0.001	0.91	0.42–1.94	0.80

Abbreviations: OR Odds Ratio, CI Confidence Interval, PS Performance Status
Hb Hemoglobin, Cr Creatinine, WBC White Blood Cell.

outpatients respectively was 8.4 months (95% CI 4.6–10.1) vs 10.6 months (95% CI 9.8–11.7), $p = 0.002$. Among untreated patients, OS for inpatients vs outpatients respectively was 1.5 months (95% CI 1.1–2.1) vs 3.9 months (95% CI 3.4–4.4), $p < 0.001$. See Fig. 1 for Kaplan-Meier survival curves.

See Table 3 for factors associated with OS. Factors significantly associated with shorter OS in the whole cohort include age ≥ 70 , constitutional symptoms, PS 3–4, weight loss, anemia, renal dysfunction, leukocytosis, thrombocytosis, time from symptom onset to diagnosis > 6 months, no systemic therapy and inpatient status at first consultation. Factors that remained significant predictors of shorter survival in multivariate analysis include constitutional symptoms, PS 3–4, leukocytosis, thrombocytosis, time from symptom onset to diagnosis > 6 months, no systemic treatment and inpatient status at first consultation.

Factors predictive of shorter OS among both treated and untreated patients in univariate analysis include constitutional symptoms, PS 3–4, weight loss $\geq 5\%$, leukocytosis, thrombocytosis, and inpatient status at first consult. Factors that remained significantly predictive of shorter OS for both groups in multivariate analysis include PS 3–4 and thrombocytosis, whereas weight loss and leukocytosis remained positive for the treated group only, and inpatient status at first consult remained positive for the untreated group only. Only in the treated group was time from symptoms to diagnosis > 6 months significantly predictive of longer OS in univariate analysis, and it remained positive in multivariate analysis.

Discussion

We performed a retrospective population-based analysis of 637 consecutive inpatients ($n = 123$) and outpatients ($n = 514$) seen as new consultations by medical oncologists at our tertiary care centre from 2009–2012. We believe this is the first direct comparison of patients presenting to medical oncologists through the inpatient vs outpatient departments with palliative stage IIIB and IV NSCLC. Of the overall cohort, 19% of new consults were seen as inpatients which represents a substantial proportion of patients. There was an *a priori* assumption that inpatients would be more unwell at baseline than their outpatient counterparts and this hypothesis was supported by our results. Inpatients unsurprisingly had worse PS, more baseline laboratory derangements, constitutional symptoms, weight loss and were more symptomatic. Symptom onset tended to be more rapid in inpatients compared to their outpatient counterparts. We can hypothesize that the more rapid symptom onset left these patients with less opportunity to pursue outpatient diagnosis, workup and/or management before becoming unwell and requiring admission to hospital.

Not surprisingly, substantially fewer inpatients received systemic

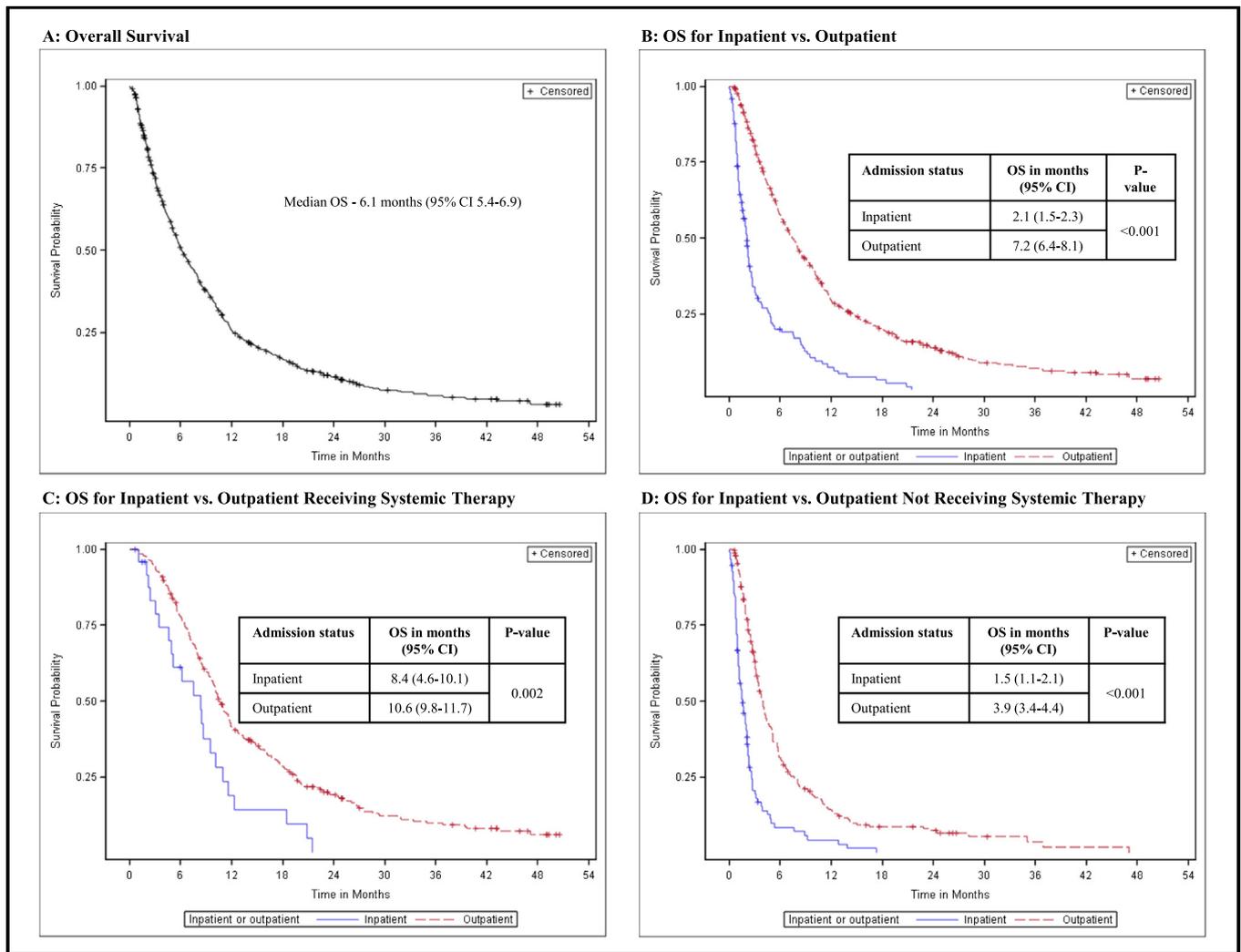


Fig. 1. Kaplan-Meier survival curves
Abbreviations: HR, Hazard ratio; CI, Confidence interval.

Table 3
Factors associated with overall survival in the overall cohort.

Factor	Univariate analysis			Multivariate analysis		
	HR	95% CI	P-value	HR	95% CI	P-value
Age ≥ 70	1.26	1.06–1.49	0.008	1.17	0.93–1.48	0.18
Constitutional symptoms	1.97	1.62–2.39	<0.001	1.48	1.11–1.96	0.007
PS 3–4	3.37	2.76–4.10	<0.001	1.68	1.24–2.28	0.001
Weight loss ≥ 5%	1.80	1.45–2.16	<0.001	1.16	0.90–1.49	0.27
Hb < 100	1.64	1.21–2.20	0.001	0.89	0.57–1.40	0.62
LDH ≥ 250 ^a	1.51	1.09–2.11	0.014			
Cr ≥ 120	1.38	1.03–1.86	0.031	0.94	0.64–1.37	0.74
WBC ≥ 11	1.69	1.42–2.01	<0.001	1.44	1.13–1.83	0.003
Platelets ≥ 400	1.68	1.38–2.02	<0.001	1.64	1.27–2.12	0.001
Time from symptoms to diagnosis						
< 2 weeks	Ref			Ref		
2–6 weeks	0.93	0.65–1.32	0.67	1.08	0.68–1.7	0.75
6 weeks–6 months	0.83	0.61–1.13	0.24	0.74	0.48–1.13	0.16
> 6 months	0.62	0.44–0.88	0.007	0.63	0.40–0.99	0.05
Time from diagnosis to consultation	0.997	0.996–0.999	<0.001	0.996	0.994–0.997	<0.001
Time from diagnosis to treatment	0.997	0.996–0.999	<0.001			
No systemic treatment	2.75	2.31–3.27	<0.001	2.13	1.65–2.75	<0.001
Inpatient at first consult	3.08	2.48–3.83	<0.001	1.61	1.13–2.29	0.009

Abbreviations: HR Hazard Ratio, CI Confidence Interval, PS Performance Status, Hb hemoglobin, LDH Lactate Dehydrogenase, Cr Creatinine, WBC white blood cell.
^a Excluded from multivariate analysis due to insufficient numbers.

therapy (21% of inpatients vs 55% of outpatients). Previous data have demonstrated that only 70% of patients with advanced lung cancer have at least one consultation with a medical oncologist [2] primarily due to poor functional status, rapid decline, and patient wishes, [8] so actual treatment rates may be even lower than our results suggest. In the present analysis, when analyzing patients well enough for treatment, compared to outpatients who received systemic therapy, inpatients who received systemic therapy were younger and more clinically unwell. Inpatients had more rapid onset of symptoms signifying potentially more clinically aggressive disease. Surprisingly, inpatients who received systemic therapy were more likely to have a complete or partial response based on RECIST criteria [7] than their outpatient counterparts. Previous literature, in contradiction with our results, suggests that younger age and worse performance status are associated with lower likelihood of objective response [9]. This may suggest that tumour factors, and clinician judgement of who may benefit, rather than baseline demographics are the likely cause of improved response in our inpatient cohort.

Among patients who received systemic therapy, OS for inpatients began to approach that of their outpatient counterparts (8.4 vs 10.6 months, $p = 0.002$). While statistically significant, this absolute difference of 2.2 months may not be clinically relevant given how sick the hospitalized population was at the beginning, and actually represents a very reasonable survival time. Given this, it is perhaps unsurprising that inpatient status was not a predictor of decreased survival in multivariate analysis among treated patients, suggesting that treated inpatients fared slightly less well due to poorer baseline prognostic factors rather than an admission status. In contrast, we must acknowledge that the group of inpatients who received systemic therapy were likely highly selected, deemed fit enough for treatment and therefore likely represented the most robust subset of the inpatient group. That said, these results suggest that inpatient status at presentation to medical oncology should not be deemed a deterrent for systemic therapy. We have previously shown at our institution that patients with a variety of malignancies who received systemic therapy while admitted to hospital had a median OS of only 4.5 months, and in the NSCLC cohort the OS was even shorter at 2.5 months [10]. This suggests that location of chemotherapy delivery in the inpatient vs outpatient departments may influence outcomes (due to patient selection), however such an analysis was beyond the scope of the present work.

Not surprisingly, untreated outpatients had a better OS than inpatients (3.9 vs 1.5 months, $p < 0.001$), indicating that inpatients who are too unwell for systemic therapy are likely nearing the end of life at the time of presentation to medical oncology. The very short OS of 1.5 months in this group of patients may be explained by the observations of Seow and colleagues [11]. Using a palliative performance scale (PPS) score [12] based on a patient's level of ambulation, activity level, evidence of disease, ability to do self-care, oral intake, and level of consciousness, Seow et al. showed that the trajectory of the average PPS score in advanced cancer decreased slowly over time until the last months of life when the PPS score decreased much more rapidly. As such, it is likely that patients requiring admission who are too unwell to receive systemic therapy are already undergoing a terminal functional decline. This is supported by a study showing that patients with advanced lung cancer suffer frequent and severe symptoms that worsen in the final months of life [13]. The very short survival of these patients in our cohort highlights the need for rapid institution of palliative care and end of life care services.

Limitations of this study include its retrospective nature and single-institution setting. Future directions should include the development of community-based strategies to improve the rapidity of diagnosis and referral of lung cancer patients to medical oncology prior to a terminal functional decline and defining criteria for the identification of

inpatients well enough for systemic therapy. Developing prognostic scores such as those developed for patients entering phase I trials may be an avenue to explore [14,15].

Conclusions

Patients presenting to medical oncologists through the inpatient department were more unwell with clinically more aggressive disease. Not surprisingly, fewer received systemic therapy, but among those who did, they were more likely to respond when compared to their outpatient counterparts and their OS began to approach that of the outpatient cohort. Systemic therapy should therefore be a consideration in select patients presenting to medical oncologists through the inpatient department and we must strive to develop criteria to help us identify those most likely to benefit while minimizing harm.

Acknowledgements

None

Sources of support

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

- [1] Canadian Cancer Society's Advisory Committee on Cancer Statistics, Canadian Cancer Statistics 2016 Toronto, On: Canadian Cancer Society, 2016.
- [2] AG Sacher, LW Le, A Lau, CC Earle, NB Leighl, Real-world chemotherapy treatment patterns in metastatic non-small cell lung cancer: are patients undertreated? *Cancer* 121 (15) (2015) 2562–2569.
- [3] J Barrett, W. Hamilton, Pathways to the diagnosis of lung cancer in the UK: a cohort study, *BMC Fam. Pract.* 9 (2008) 31.
- [4] J Gotfrit, T Zhang, S Zanon-Heacock, P Wheatley-Price, Patients with advanced non-small cell lung cancer requiring inpatient medical oncology consultation: characteristics, referral patterns, and outcomes, *Clin. Lung Cancer* 17 (4) (2016) 292–300.
- [5] SY Brule, K Al-Baimani, H Jonker, T Zhang, G Nicholas, G Goss, et al., Palliative systemic therapy for advanced non-small cell lung cancer: investigating disparities between patients who are treated versus those who are not, *Lung Cancer* 97 (2016) 15–21.
- [6] MM Oken, RH Creech, DC Tormey, J Horton, TE Davis, ET McFadden, et al., Toxicity and response criteria of the Eastern Cooperative Oncology Group, *Am. J. Clin. Oncol.* 5 (6) (1982) 649–655.
- [7] EA Eisenhauer, P Therasse, J Bogaerts, LH Schwartz, D Sargent, R Ford, et al., New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1), *Eur. J. Cancer* 45 (2) (2009) 228–247.
- [8] JJ Ko, R Tudor, H Li, M Liu, K Skolnik, WK Boland, et al., Reasons for lack of referral to medical oncology for systemic therapy in stage IV non-small-cell lung cancer: comparison of 2003–2006 with 2010–2011, *Curr. Oncol.* 24 (6) (2017) e486–e493.
- [9] TF Hickish, IE Smith, ME O'Brien, S Ashley, G Middleton, Clinical benefit from palliative chemotherapy in non-small-cell lung cancer extends to the elderly and those with poor prognostic factors, *Br. J. Cancer* 78 (1) (1998) 28–33.
- [10] P Wheatley-Price, M Ali, K Balchin, J Spencer, E Fitzgibbon, C Cripps, The role of palliative chemotherapy in hospitalized patients, *Curr. Oncol.* 21 (4) (2014) 187–192.
- [11] H Seow, L Barbera, R Sutradhar, D Howell, D Dudgeon, C Atzema, et al., Trajectory of performance status and symptom scores for patients with cancer during the last six months of life, *J. Clin. Oncol.* 29 (9) (2011) 1151–1158.
- [12] F Anderson, GM Downing, J Hill, L Casorso, N Lerch, Palliative performance scale (PPS): a new tool, *J. Palliat. Care* 12 (1) (1996) 5–11.
- [13] S Lutz, R Norrell, C Bertuccio, I Kachnic, C Johnson, D Arthur, et al., Symptom frequency and severity in patients with metastatic or locally recurrent lung cancer: a prospective study using the Lung Cancer Symptom Scale in a community hospital, *J. Palliat. Med.* 4 (2) (2001) 157–165.
- [14] NG Chau, A Florescu, KK Chan, L Wang, EX Chen, P Bedard, et al., Early mortality and overall survival in oncology phase I trial participants: can we improve patient selection? *BMC Cancer* 11 (2011) 426.
- [15] HT Arkenau, J Barriuso, D Olmos, JE Ang, J de Bono, I Judson, et al., Prospective validation of a prognostic score to improve patient selection for oncology phase I trials, *J. Clin. Oncol.* 27 (16) (2009) 2692–2696.